

### REMARKS

Upon entry of the present amendment, claims 11, 169-173, 175, 178, 179 and 181-208 will be pending and under examination. Claims 176 and 180 have been cancelled. Claims 11, 170, 174, 175, 177, 178, 179, 191 and 194 have been amended.

The Applicants thank Examiner Zeman for the courtesy of the telephone interview conference conducted on December 20, 2005. The Applicants' representatives discussed with the Examiner the following grounds for rejection raised in the Office Action of November 15, 2005: (a) provisional double patenting rejection; (b) indefiniteness rejection of claim 11 due to its structure; and (c) new matter rejection of claims 11 and 191 due to presence of "one or more acetylated amino acid side chains" language. The Applicants' position is further elaborated below.

### Claim Objections

The Applicants have amended claim 194 to correct a typographical error identified by the Examiner.

### Rejections for Double Patenting

The Examiner rejected claims 1, 171, 173, 179, 181-189, 191-194 and 207-208 as follows:

Claims 1, 171, 173, 179, 181-185, 188-189, 191-194 and 207-208 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 118-130 of copending Application No. 09/735,786.

The Examiner further stated:

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The Applicants do not accede to the substance of this rejection. As noted by the Examiner this is a provisional rejection over the co-pending application 09/735,786. Accordingly, the Applicants request that the Examiner follow the procedures elaborated in MPEP § 804.I.B, which authorizes advancing one application to issuance where a provisional

double patent rejection is made between two pending applications. The section states in particular:

The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent. [emphasis added]

Based on the present amendment, the Applicants expect that this provisional double patenting rejection will be "the only rejection remaining" in this application. The Examiner of 09/735,786 will be notified of the double patent rejection made in this application. The Applicants note that the 09/735,786 case has yet to be examined, despite Applicants' inquiries. Further, this application has an earlier filing date than 09/735,786. Accordingly, the double patent rejection made in this application should be withdrawn so that, of the two, this application may be the first to issue as a patent.

### **Rejections under 35 U.S.C. § 112**

The Examiner rejected claims 11, 169-190 and 194-206 as indefinite. These rejections are addressed in turn below:

Claims 11, 169-190, 194-206 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is rejected as being rendered vague and indefinite by the language set forth in the preamble of the claim and in step a) of the recited method. It is unclear, whether Sir 2 is necessarily present in the reaction mixture.

The Applicants have amended claim 11 to clarify that Sir2 protein is present in the reaction mixture. Because claims 169-175, 177-179, 181-190 and 194-206 depend from claim 11, present amendment of claim 11 likewise places these dependent claims in condition for allowance.

Claim 176 is rendered vague and indefinite by the recitation of specific amino acid residues (lysine 9 and lysine 14) without providing a base sequence.

Claim 180 is rendered vague and indefinite by the recitation of specific amino acid residues (lysine 16) without providing a base sequence.

The Applicants have cancelled claims 176 and 180 without prejudice, rendering rejections of these two claims moot.

Further, the Examiner rejected claims 11 and 169-208 as follows:

Claim 11 and 169-208 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended claims 11 and 191 to recite "... one or more acetylated amino acid side chains ...". This phrase does not appear in the specification, or original claims as filed. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Therefore this limitation is new matter.

Although the Applicants respectfully disagree, the Applicants have amended claims 11 and 191 to recite "a histone protein or an N-terminal fragment thereof that comprises an acetylated amino acid side chain," and "determining if the histone protein or the N-terminal fragment thereof is deacetylated." This amendment should moot the Examiner's rejection.

The application describes, *inter alia*, evaluating NAD-dependent acetylation status of histone proteins. For example, the application discloses that "Sir2 (e.g., murine Sir2 $\alpha$ ) alters the NAD-dependent acetylation status (e.g., removes and/or adds an acetyl group) of histone proteins" (at page 15, lines 25-27). The application also specifies that "[t]he modification of the acetylation status of the N-terminal tails of histones by Sir2 can trigger genomic silencing in yeast and heterochromatin formation more generally in eukaryotic organisms" (at page 53, lines 19-22). The application includes, among its examples, a description of determining the deacetylation of a histone N-terminal fragment (at page 76, lines 17-23).

Nor does this amendment raise concerns expressed by the Examiner in the Office Action dated March 26, 2004. In that Action, the Examiner stated "It is unclear which specific 'side chain' Applicant is referring to if the claimed composition contains more than one acetylated amino acid side chains." The open-ended language includes histones and N-terminal histone fragments that have plural acetylated amino acid side chains. The step of determining if the

histone or N-terminal histone fragment is deacetylated refers to deacetylation of any of the acetylated amino acid side chains. For example, methods are available and described in the application for determining deacetylation even without resolving which particular side chain is deacetylated.<sup>1</sup> See, e.g., FIG. 9 (mass spectroscopy and HPLC chromatography) FIG. 12 (HPLC chromatography). In many cases, where an "agent to be tested" is evaluated, as in the method of claim 11, it is sufficient to determine if the histone or N-terminal fragment is deacetylated. No further information is needed to evaluate whether the agent inhibits or activates Sir2 protein.

The Applicants respectfully request that all 35 U.S.C. § 112 rejections be withdrawn and all the claims expeditiously allowed.

### **Conclusion**

The Applicants respectfully submit that all claims are in condition for allowance, which action is expeditiously requested. The Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do the Applicants concede that there are not other good reasons for patentability of the presented claims or other claims. All amendments and withdrawals are made without prejudice and disclaimer.

Enclosed is a Petition for Extension of Time. Please apply any charges or credits to deposit account 06-1050, referencing Attorney's Docket Number 13407-016001.

Respectfully submitted,

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<sup>1</sup> Of course, methods are also available and described for determining which side chain is deacetylated. For example, Edman degradation (FIG. 10).